Medical Policy:

Spinraza (nusinersen)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.33C	January 4, 2024	July 18, 2019

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Spinraza is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide indicated for the treatment of spinal muscular atrophy (SMA). The drug is administered intrathecally.

Spinal muscular atrophy (SMA) is neurological disease characterized by loss of motor neurons in the spinal cord and lower brain stem, resulting in severe and progressive muscular atrophy and weakness. 5q-SMA is an autosomal recessive genetic disorder caused by mutations in the SMN1 (survival motor neuron) gene that is found on chromosome 5. To develop SMA, an individual must inherit two faulty SMN1 genes, one from each parent.

SMA Type	Age at Onset	Features/Clinical Presentation	Lifespan	SMN2 Copy Gene Number
0	Prenatal	Severe hypotonia and weakness; respiratory failure at birth. There is no achievement of motor milestones.	A few weeks to < 6 months	0 to 1
1	< 6 months	Poor muscle tone, lack of movement, and respiratory assistance needed at birth. Patients are never able to sit.	< 2 years	1 to 2
2	Before 18 months	Patients are able to sit. However, patients are unable to walk or stand without assistance.	75% of patients are alive at 25 years of age	2 to 3
3	> 18 months	Walks independently but may lose this ability as the disease progresses.	Normal	3 to 4
4	Adulthood	Walk until adulthood.	Normal	≥ 4

SMA – Spinal muscular atrophy; SMN2 – Survival motor neuron 2.

Length of Authorization

Initial: 2 months

Renewal: 12 months

Dosing Limits [Medical Benefit]

Quantity Limit:

Loading: 1 vial on Day 1, Day 15, Day 29, and Day 59

Maintenance: 1 vial every 112 days

Max Units (per dose and over time) [HCPCS Unit]:

Loading: 120 billable units on Day 1, Day 15, Day 29, and Day 59

Maintenance: 120 billable units every 112 days

Guideline

Spinraza is considered medically necessary for the treatment of Types I, II or III SMA in pediatric and adult patients when the following criteria are met.

A. Initiation therapy; all:

1. Diagnosis of SMA by, or in consultation with a neurologist with expertise of SMA; **AND**
2. Spinraza is being prescribed by, or in consultation with a neurologist with expertise of SMA; **AND**
3. Clinical documentation of 5q SMA homozygous gene mutation, homozygous gene deletion or compound heterozygote (i. or ii, **AND** iii.)
   i. Homozygous gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13); **OR**
   ii. Compound heterozygous mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2])

   AND

   iii. Patient has Documentation of genetic testing confirming at least 2 copies of SMN2; **AND**
4. Baseline exam of at least **ONE** of the following exams to establish baseline motor ability:
   i. Hammersmith Infant Neurological Exam (HINE) (infant to early childhood); **OR**
   ii. Hammersmith Functional Motor Scale Expanded (HFMSE); **OR**
   iii. Upper Limb Module (ULM) Test (Non ambulatory); **OR**
   iv. Revised Upper Limb Module (RULM), **OR**
   v. Bayley Scales of Infant and Toddler development Third Ed. (BSID-III), **OR**

vi. 6-minute walk test (6MWT), **OR**

vii. Motor Function Measure 32 (MFM32) **OR**

viii. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND); **AND**

5. Patient is **NOT** dependent on either invasive ventilation or tracheostomy, **OR** Non-invasive ventilation for at least 12 hours per day; **AND**
6. Patient has not previously received gene replacement therapy for the treatment of SMA; **AND**
7. Spinraza is to be administered intrathecally by, or under the direction of, healthcare professionals experienced in performing lumbar punctures; **AND**
8. Spinraza dosing is in accordance with the United States Food and Drug Administration approved labeling: maximum dosing of 12mg for each loading dose; **AND**
9. Initial authorization will be for no more than 4 loading doses

B. Continuation therapy ; all:

1. SMA diagnosis and treatment prescription by, or in consultation with, a neurologist; **AND**
2. Patient continues to meet ALL of the initial criteria requirements outlined above; **AND**
3. Absence of unacceptable toxicity which would preclude safe administration of the drug. *(Examples of unacceptable toxicity include: significant renal toxicity, thrombocytopenia, coagulation abnormalities, etc.)*; **AND**
4. Patient has responded to therapy compared to pretreatment baseline in **ONE** or more of the following:

    A. Stability or improvement in net motor function/milestones, including but not limited to, the following validated scales: Hammersmith Infant Neurologic Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), Bayley Scales of Infant and Toddler development Third Ed. (BSID-III), 6-minute walk test (6MWT), Upper Limb Module (ULM), Motor Function Measure 32 (MFM32), Revised Upper Limb Module (RULM), etc; **OR**

    B. Stability or improvement in respiratory function tests [e.g., forced vital capacity (FVC), etc.]; **OR**

    C. Reduction in exacerbations necessitating hospitalization and/or antibiotic therapy for respiratory infection in the preceding year/timeframe; **OR**

    D. Stable or increased patient weight (for patients without a gastrostomy tube); **OR**

    E. Slowed rate of decline in the aforementioned measures

Limitations/Exclusions

Spinraza is not considered medically necessary for any indication other than as listed above.

***EmblemHealth considers Spinraza not medically necessary for individuals in current treatment or previously treated with gene therapy (e.g. Zolgensma) for SMA.**

Applicable Procedure Codes

Code	Description
J2326	Injection, nusinersen, 0.1 mg (Eff. 01/01/2018)

Applicable NDCs

Code	Description
64406-0058-01	SPINRAZA 12MG/5ML Solution J2326 Injection, nusinersen, 0.1 mg

ICD-10 Diagnoses

Code	Description
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffman]
G12.1	Other inherited spinal muscular atrophy
G12.25	Progressive spinal muscle atrophy
G12.8	Other spinal muscular atrophies and related syndromes
G12.9	Spinal muscular atrophy, unspecified

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/4/2024	Annual Review: Initial Criteria: Added additional scales that are able to be used: "Revised Upper Limb Module (RULM), OR Bayley Scales of Infant and Toddler development Third Ed. (BSID-III), OR 6-minute walk test (6MWT), OR Motor Function Measure 32 (MFM32) OR" Continuation therapy Removed: "No respiratory dependency on either: Invasive ventilation or tracheostomy, Non-invasive ventilation for a period ≥ 6 hours per day , Prevention of permanent ventilation (≥ 16 hours ventilation/day continuously for> 21 days in absence of an acute reversible event or tracheostomy) " and "Clinical documentation delineates positive therapeutic response to Spinraza, from pretreatment baseline, as demonstrated by any of the measurement tools (a, b, c, or d, as appropriate) (Physician evaluation must occur ≤ 1 month prior to request) Hammersmith Infant Neurological Examination (HINE) milestones (for infants 2 months–2 years of age (i and ii): One of the following: Improvement, or maintenance of previous improvement, of at least 2 point (or maximal score) increase in ability to kick, Improvement, or maintenance of previous improvement, of at least 1 point increase in any other HINE milestone (e.g., head control, rolling, sitting, crawling, etc.), excluding voluntary grasp One of the following: Improvement or maintenance of previous improvement in more HINE motor milestones than worsening, from pretreatment baseline (net positive improvement), Member achieved and maintained any new motor milestones that is otherwise not expected (e.g., sit unassisted, stand, walk) Hammersmith Functional Motor Scale (HFMSE): (i. or ii.) Improvement, or maintenance of previous improvement, of at least a 3 point increase in score from pretreatment baseline Member has achieved and maintained any new motor milestone from pretreatment baseline that is otherwise not expected Upper Limb Module (ULM): (i. or ii.) Improvement or maintenance of previous improvement of at least a 2 point increase in score from pretreatment baseline Member has achieved and maintained any new motor milestone from pretreatment baseline that is otherwise not expected Children's Hospital of Philadelphia (CHOP) infant Test of Neuromuscular Disorders (INTEND): (i. or ii.) Improvement, or maintenance of previous improvement, of at least a 4 point increase in score from pretreatment baseline Member has achieved and maintained any new motor milestone from pretreatment baseline that is otherwise not expected"

		Added: "Absence of unacceptable toxicity which would preclude safe administration of the drug. *(Examples of unacceptable toxicity include: significant renal toxicity, thrombocytopenia, coagulation abnormalities, etc.)*; AND Patient has responded to therapy compared to pretreatment baseline in ONE or more of the following: Stability or improvement in net motor function/milestones, including but not limited to, the following validated scales: Hammersmith Infant Neurologic Exam (HINE), Hammersmith Functional Motor Scale Expanded (HFMSE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), Bayley Scales of Infant and Toddler development Third Ed. (BSID-III), 6-minute walk test (6MWT), Upper Limb Module (ULM), Motor Function Measure 32 (MFM32), Revised Upper Limb Module (RULM), etc, Stability or improvement in respiratory function tests [e.g., forced vital capacity (FVC), etc.], Reduction in exacerbations necessitating hospitalization and/or antibiotic therapy for respiratory infection in the preceding year/timeframe, Stable or increased patient weight (for patients without a gastrostomy tube), Slowed rate of decline in the aforementioned measures" Added code G12.25
EmblemHealth & ConnectiCare	4/27/2023	Annual Review: Updated dose limits: Removed: Initial: 4 vials for the first 58 days Maintenance: 1 vial every 120 days Added: Loading: 1 vial on D1, D15, D29, and D59 Maintenance: 1 vial every 112 days **Max Units (per dose and over time) [HCPCS Unit]:** Loading: 120 billable units on D1, D15, D29, and D59 Maintenance: 120 billable units every 112 days Updated definition to include SMA Type 0: Removed: SMA Type 1 (infantile onset SMA or Werdnig-Hoffmann disease) — symptoms are present at birth or by the age of 6 months SMA Type 2 — onset of symptoms between the ages of 7 and 18 months and before the child can stand or walk independently SMA Type 3 — onset of symptoms after 18 months, and children can stand and walk independently, although they may require aids SMA Type 4 (adult-onset SMA or Kugelberg-Welander disease) — onset of symptoms in adulthood, and people are able to walk during their adult years. Added: chart with SMA Types Removed codes J3490 and J3590 Removed the following from the initial criteria: "Both of the following: i. Patient has previously received gene replacement therapy; **AND** ii. Patient has experienced a declination in clinical status that represented a potential failure or abatement of gene therapy efficacy; **AND"**
EmblemHealth & ConnectiCare	1/12/2023	Transfer to New Template
EmblemHealth & ConnectiCare	8/6/2020	Updated package insert hyperlink to reflect current PI - Updated Guideline to include "pediatric and adult patients" - Removed pediatric neurologist requirement, changed prescriber requirement to "prescribed by, or in consultation with a neurologist who specializes in SMA"

		- Updated genetic testing requirement from “no more than 2 copies of SMN2” to “at least two copies of SMN2” - Removed age requirement - Added requirements around previous gene therapy - Continuation Criteria - added statement: Patient continues to meet ALL of the initial criteria requirements outlined above - Updated duration of initial approval from 6 months to 2 months - Updated duration of renewal approval from 6 months to 12 months
EmblemHealth & ConnectiCare	7/18/2019	Added statement: Emblem Health considers Spinraza not medically necessary for individuals in current treatment or previously treated with gene therapy (e.g. Zolgensma) for SMA

References

1. Med Lett Drugs Ther. 2017 Mar 27;59(1517):50-52. Nusinersen (Spinraza) for spinal muscular atrophy.
2. Nat Neurosci. 2017 Apr;20(4):497-499. doi: 10.1038/nn.4508. Epub 2017 Feb 13. Nusinersen, an antisense oligonucleotide drug for spinal muscular atrophy. Corey DR.
3. Neurology. 2016 Mar 8;86(10):890-7. doi: 10.1212/WNL.0000000000002445. Epub 2016 Feb 10. Results from a phase 1 study of nusinersen (ISIS-SMN(Rx)) in children with spinal muscular atrophy. Chiriboga CA1, Swoboda KJ2, Darras BT2, Iannaccone ST2, Montes J2, De Vivo DC2, Norris DA2, Bennett CF2, Bishop KM2.
4. Specialty matched clinical peer review.
5. Spinraza [Prescribing Information] Cambridge, MA: Biogen; December 2016.